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Prenatal alcohol exposure alters the patterns of facial asymmetry

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Abstract

Directional asymmetry, the systematic differences between the left and right body sides, is widespread in human populations. Changes in directional asymmetry are associated with various disorders that affect craniofacial development. Because facial dysmorphology is a key criterion for diagnosing fetal alcohol syndrome (FAS), the question arises whether in utero alcohol exposure alters directional asymmetry in the face. Data on the relative position of 17 morphologic landmarks were obtained from facial scans of children who were classified as either FAS or control. Shape data obtained from the landmarks were analyzed with the methods of geometric morphometrics. Our analyses showed significant directional asymmetry of facial shape, consisting primarily of a shift of midline landmarks to the right and a displacement of the landmarks around the eyes to the left. The asymmetry of FAS and control groups differed significantly and average directional asymmetry was increased in those individuals exposed to alcohol in utero. These results suggest that the developmental consequences of fetal alcohol exposure affect a wide range of craniofacial features in addition to those generally recognized and used for diagnosis of FAS.

Keywords: Directional asymmetry; Discriminant function; Facial dysmorphology; Fetal alcohol syndrome; Procrustes superimposition

Introduction

Directional asymmetry is defined as systematic differences between the left and right sides of the body. Examples are the conspicuous asymmetry of internal organs and the more subtle asymmetry of the human brain (e.g., Toga and Thompson, 2003). With the advent of powerful methods of geometric morphometrics, it has become apparent that subtle, but significant directional asymmetry is nearly ubiquitous even for apparently symmetric features, such as craniofacial features or limbs and is found in a wide range of organisms (Auffray et al., 1996; Klingenberg, 2002; Klingenberg et al., 1998, 2002), including humans (e.g., DeLeon, 2007; Ercan et al., 2008; Schaefer et al., 2006).

Although subtle facial directional asymmetry is present in healthy individuals (DeLeon, 2007; Ercan et al., 2008; Schaefer et al., 2006), stronger directional asymmetry is often associated with conditions that disrupt normal craniofacial development, such as cleft lip and palate (Bock and

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Bowman, 2006), deformational plagiocephaly, or craniosynostosis (Netherway et al., 2006). Changed patterns of directional asymmetry have been reported among individuals diagnosed with disorders in which facial changes may be a secondary consequence of abnormal brain development, such as schizophrenia (Hennessy et al., 2004) and autism spectrum disorder (Hammond et al., 2008).

Specific facial dysmorphology, resulting from prenatal exposure to alcohol, remains the key diagnostic feature of fetal alcohol syndrome (FAS) (Astley and Clarren, 2000; Hoyme et al., 2005). Anthropometric measurements of facial changes have been shown to correctly distinguish FAS from non-FAS in different ethnic populations (Moore et al., 2007). In addition, modern techniques of geometric morphometrics have confirmed that prenatal alcohol exposure has significant effects on facial shape (Mutsvangwa and Douglas, 2007). Thus far, little attention has been paid to the effects of prenatal alcohol exposure on facial asymmetry, although Kieser (1992) reported that maternal alcohol consumption correlates with fluctuating asymmetry in the teeth of children. Although asymmetry is normal in most populations (Ercan et al., 2008; Kimmerle and Jantz, 2005; McIntyre and Mossey, 2002; Shaner et al., 2000), no study has investigated the effects of prenatal exposure to alcohol on directional asymmetry.

Here, we report changes in the pattern of directional asymmetry among individuals prenatally exposed to alcohol and those who were not exposed. We have included ethnically distinct samples (Moore et al., 2007). We used sensitive morphometric methods specifically developed for measuring asymmetry of shape (Bock and Bowman, 2006; Klingenberg and McIntyre, 1998; Klingenberg et al., 2002). These methods detected subtle, but statistically significant, directional asymmetry in the face and revealed that asymmetry is not the same for individuals who were prenatally exposed to alcohol as compared with those without prenatal alcohol exposure.

Material and methods

Study design

Participants were assessed as part of an ongoing international consortium, the Collaborative Initiative on Fetal Alcohol Spectrum Disorders (CIFASD). Participants were from two sites: Cape Town, South Africa and Helsinki, Finland. This study was approved by the Institutional Review Board at each site and at the grantee institutions (Indiana University School of Medicine, Wayne State University School of Medicine, and Biomedical Sciences, San Diego State University). All participants and/or their parent(s)/legal guardian(s) provided written informed consent and assent.

As part of the study visit, each participant was examined by members of the CIFASD Dysmorphology Core, who completed a standardized, uniform assessment as described by Jones et al. (2006). Details of the study visit are provided by Moore et al. (2007). Briefly, a standard classification system, based solely on structural features and growth deficiency, was used to determine a preliminary classification of FAS, not FAS, or deferred (Hoyme et al., 2005; Jones et al., 2006). Analyses were limited to participants with either a diagnosis of FAS from the Dysmorphology Core, or to participants with a diagnosis of ‘‘control’’ from the Dysmorphology Core who were not exposed to alcohol during pregnancy, according to maternal interview data. Individuals who were known to have been exposed to alcohol in utero but did not receive a diagnosis of FAS were labeled ‘‘deferred.’’ Because the focus of this article was to determine whether asymmetry differs between individuals with FAS and controls that were not exposed to alcohol, we excluded these deferred individuals from the current analyses. Due to potential differences in morphometric facial structure between ethnicities and sample size considerations, only participants reported to be Finnish Caucasian (FC: 40 FAS, 50 control) or Cape Coloured (CC: 49 FAS, 29 control) were included in the analysis. Demographic data are provided in Table 1.

Collection of 3-dimensional (3D) images

Facial images were captured using a commercially available laser scanner, the Minolta Vivid 910fw (Konica Minolta Sensing Americas, Inc., Boulder, CO). The scanner shines a low-intensity ‘‘eye safe’’ laser on the participant. Details describing calibration assessment of the scanners are provided by Moore et al. (2007). Participants were seated approximately 660 mm from the scanner and a trained operator located seven soft-tissue landmarks (bilateral: frontotemporale, tragion, gonion; unilateral: menton) by inspection and/or palpation, and marked them on the skin using an eye-liner pencil. Two frontal and two lateral left and right scans were obtained for each subject. For the lateral scans, the participant faced at near right angles to the scanner. Collected images were processed using a commercially available software package, Rapidform™ 2006 (INUS Technology Incorporated, Seoul, Korea).

Image processing and measurement

Rapidform™, a reverse modeling software package that scans physical objects and creates a digital version of the object, was used to merge the best lateral and frontal scans into a single, 3D model of the participant’s face. For each subject, the better of the two scans of each of the three positions was determined such that neutral expressions were present in all scans, lighting was optimal, and the number of visible landmarks was maximized. Each 3D facial image was analyzed using a customized software plug-in, written by one of the authors (J.R.) using Visual C++ and the Rapidform™ application programming interface. An